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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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27916	7590	11/07/2006	EXAMINER	
VERTEX PHARMACEUTICALS INC. 130 WAVERLY STREET CAMBRIDGE, MA 02139-4242			BALASUBRAMANIAN, VENKATARAMAN	
			ART UNIT	PAPER NUMBER

1624

DATE MAILED: 11/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

10/696,862

Applicant(s)

CAO ET AL.

Examiner

Venkataraman  
Balasubramanian

Art Unit

1624

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 19 October 0206 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: 1-46.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 47-53.  
Claim(s) withdrawn from consideration: 54-56.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

Venkataraman Balasubramanian  
Venkataraman Balasubramanian  
Primary Examiner  
Art Unit: 1624 11/1/06

### **ADVISORY ACTION**

The applicants' response, which included amendment to claims 1, 9, 10, 24, 34-37, 42, 45, 47, 48, 50, 51, and 53, filed 10/19/2006 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance for the following reasons.

In view of applicants' response, the 112 second paragraph rejections and 103 rejection over Santora et al. have deemed as obviated. However, the following 112 first paragraph rejection made in the previous office action is maintained. In addition, new grounds of rejections are applied as necessitated by applicants' amendment.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of obesity embraced, does not reasonably provide enablement for treating or lessening the severity of any or all diseases and disorder embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims 47-53 are drawn to method of inhibiting various kinases as well as treating various diseases and disorders and claim 46 drawn to a composition with intended use for treating various diseases.

Claims 47-53 are reach through claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification.

In the instant case, because of the interaction of the compound formula I with various kinases, it is recited that instant compounds are useful for treating or lessening the severity of any or all disorders and diseases selected from a proliferative disorder, a cardiac disorder, a neurogenerative disorder, a psychotic disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, viral disease, or a bone disorder for which there is no adequate written description and enabling disclosure in the instant specification. The scope of the claims includes any or all disorders/ diseases due to kinase activity (such as Rock, ERK2, GSK, AGC etc.) inhibition including those yet to be discovered as due said mode of action for which there is no enabling disclosure. In addition, the scope of these claims includes treating or lessening severity of various disorders and diseases that include a proliferative disorder, a cardiac disorder, an inflammatory disorder, an autoimmune disorder, a viral disease, or a bone disorder each of which would include any number diseases or disorders. For example proliferative disorders can include any cancer such as lung cancer, bone cancer, pancreatic cancer, skin cancer. cancer of the head or neck, cutaneous or intraocular melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region. stomach cancer, colon cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium,

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carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's disease, cancer of the esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, prostate cancer, chronic or acute leukemia, lymphocytic lymphomas, cancer of the bladder, cancer of the kidney or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system (CNS), primary CNS lymphoma, spinal axis tumors, brain stem glioma, pituitary adenoma, or a combination of one or more of the foregoing cancers. List of the other disorders would of course add to this huge list of diseases, as well as those specifically claimed such as allergy, asthma, diabetes, Alzheimer's disease, Huntington's disease, Parkinson's disease, Ams-associated dementia, amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease), multiple sclerosis (MS), schizophrenia, cardiomyocyte hypertrophy, reperfusion/ischemia, stroke, or baldness, various other neurodegenerative or neurological disorder, which are not adequately enabled solely based on the activity of the compounds provided in the specification. The instant compounds are disclosed to have kinase inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all diseases stated above for which applicants provide no competent evidence. It appears that the applicants are asserting that the embraced compounds because of their mode of action as kinase inhibitor shown in examples of pages 151-153, that would be useful for all sorts of disorders and diseases. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the

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uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of neurological diseases, autoimmune diseases, proliferative diseases are very difficult to treat and despite the fact that there are many drugs with the same mode of action..

The scope of the claims involves thousands of compounds of claim 1 as well as the thousand of diseases embraced by the term disorder and disease

No compound has ever been found to treat all types of medical conditions generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of modern medicine. Proliferative disease would include benign tumors, malignant tumors, polyps, lumps, lesions, other pre-cancerous conditions, psoriasis, leukemia, the hyper proliferation of the gastric epithelium caused by the *Helicobacter pylori* infection of ulcers.

Cancer is just an umbrella term. Tumors vary from those so benign that they are never treated to those so virulent that all present therapy is useless.

No compound has ever been found to treat proliferative diseases of all types generally. The same is true for cardiac disorder, a neurogenerative disorder, a psychotic disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, viral disease, or a bone disorder. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of oncology.

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Cecil Textbook of Medicine states, "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally. Thus, it is beyond the skill of clinician today to get an agent to be effective against cancers generally. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288. Also note *Hoffman v. Klaus* 9 USPQ 2d 1657 and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Kim et al., *Current Opinion in Genetics and Development*, 10, 508-514, 2000, Mass, R. D., *Int. J. Radiation Oncology Bio. Phys.* Vol. 58(3): 932-940, 2004 and Fabbro et al. *Pharmacology & therapeutics* 93, 79-98, 2002.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or

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lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating disorders/diseases that require receptor kinase inhibitory activity.

2) The state of the prior art: Recent publications expressed that the receptor tyrosine kinase inhibition effects are unpredictable and are still exploratory. See Mass et al. and Fabbro et al., cited above especially the concluding paragraph.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating or lessening the severity of any or all disorders and diseases selected from a proliferative disorder, a cardiac disorder, a neurogenerative disorder, a psychotic disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, viral disease, or a bone disorder embraced for the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all disorders diseases such as treating or lessening the severity of any or all disorders and

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diseases selected from a proliferative disorder, a cardiac disorder, a neurogenerative disorder, a psychotic disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, viral disease, or a bone disorder and the state of the art is that the effects of kinase inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace treating or lessening the severity of any or all disorders and diseases selected from a proliferative disorder, a cardiac disorder, a neurogenerative disorder, a psychotic disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, viral disease, or a bone disorder including those yet to be related to kinase.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

This rejection is same as made in the previous office action. Applicants' traversal is not persuasive.

First of all, as noted above, instant claims 48 and 49 are reach through claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification.

In the instant case, because of the interaction of the compound formula I with various kinases, it is recited that instant compounds are useful for treating or lessening the severity of any or all disorders and diseases selected from a proliferative disorder, a cardiac disorder, a neurogenerative disorder, a psychotic disorder, an autoimmune disorder, a condition associated with organ transplant, an inflammatory disorder, an immunologically mediated disorder, viral disease, or a bone disorder for which there is no adequate written description and enabling disclosure in the instant specification.

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As can be seen from the definition of the term "biological sample" stated in page 109 of specification, without limitation it reads on many and all types of biological samples, which can include mammals or animals and therefore, the claimed method is seen to encompass an inhibitory method wherein the compound is administered to an animal. This is further evident from the purpose of the inhibition of various kinases activity stated in specification at various places for treating various diseases. As the inhibition of kinases in a biological sample is disclosed to be useful, it implicitly reads on the inherent therapeutic methods characterized by the activity, which as per the specification includes numerous types of diseases/disorders recited in specification.

The sole testing assay provided in the specification at pages 151-152 is to test the ability of the compounds to inhibit ROCK, ERK, PKA or GSK activity using a standard enzyme system, however, applicants have not provided how this correlates with the efficacy in all types of biological samples encompassed by the instant method and their use in the various purposes wherein the inhibition activity is useful. For example, blood transfusion is the process of transferring blood or blood-based products from one person into the circulatory system of another. Blood transfusions may be seen as a procedure to treat some medical conditions, such as massive blood loss due to trauma, surgery, shock and where the red cell producing mechanism (or some other normal and essential component) fails. Similarly, an organ transplantation is the transplantation of a whole or partial organ from one body to another (or from a donor site on the patient's own body), for the purpose of replacing the recipient's damaged or failing organ with a working one from the donor site. As can be seen from the above,

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without limitation these purposes are intended for therapeutic methods and applicant has not provided competent evidence sufficient to enable the claimed method.

Therefore, the instant claim appears to be directed to the various types of therapeutic methods. As for claim 47, it clearly recites the intended use of the composition and hence it is deemed as proper to rejection claim 47 for scope of enablement.

Secondly, the references provided in the IDS still do not support treatment all diseases including various cancers. They may support for some specific diseases and limiting to such diseases will no be objected if proper nexus is shown in the references. Applicants have not shown such nexus. Some of the references clearly indicate further experimentation. For example, Mueller et al., clearly states "However, intensive investigation will be needed to clearly evaluate safety and efficacy of future ROCK inhibitors. See page 306, concluding paragraph.

Similarly, applicants argued that because Hiroka et al. teaches hypotensive effect of ROCK inhibitors, there is support for treating any or all cardiovascular diseases. This not deemed as proper nexus for treating hypertension and any or all cardiovascular diseases.

Hence, this rejection is proper and is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 48-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting GSK-3 activity in a standard enzyme assay, does not reasonably provide enablement for a method of inhibiting GSK-3 activity in a biological sample generally for the purpose of blood transfusion, organ transplantation, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claim is drawn to 'a method of inhibiting ROCK, ERK, GSK, or AGC activity in a biological sample' and the term "biological sample" as per the definition in the specification (page 21, lines 11-134 "includes, without limitation, cell cultures or extracts thereof; biopsied material obtained from a mammal or extracts thereof; and blood, saliva, urine, feces, semen, tears, or other body fluids or extracts thereof").

First, the instant claim 48 is a 'reach through' claim. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through to the corresponding therapeutic method of any or all diseases, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

As can be seen from the definition of the term "biological sample", without limitation it reads on many and all types of biological samples, which can include mammals or animals and therefore, the claimed method is seen to encompass an inhibitory method wherein the compound is administered to an animal. This is further evident from the purpose of the inhibition of GSK-3 activity stated in pages 21, lines 11-18, which includes for example, blood transfusion, organ-transplantation, etc. As the inhibition of ROCK, ERK, GSK, or AGC activity in a biological sample is disclosed to be useful for blood transfusion, organ-transplantation, etc., it implicitly reads on the inherent therapeutic methods characterized by the activity, which as per the specification includes numerous types of diseases/disorders recited in page 20

The sole testing assay provided in the specification is to test the ability of the compounds to inhibit ROCK, ERK, GSK, or AGC activity using a standard coupled enzyme system, however, there is insufficient guidance in the disclosure regarding the provided assay. First, the specification provides that the coupled enzyme system is provided in Fox et al., however, the cited article deals with inhibition of p38 MAP kinase activity. Next, applicant has not provided how this correlates with the efficacy in all

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types of biological samples encompassed by the instant method and their use in the various purposes wherein the inhibition activity is useful. For example, blood transfusion is the process of transferring blood or blood-based products from one person into the circulatory system of another. Blood transfusions may be seen as a procedure to treat some medical conditions, such as massive blood loss due to trauma, surgery, shock and where the red cell producing mechanism (or some other normal and essential component) fails. Similarly, an organ transplantation is the transplantation of a whole or partial organ from one body to another (or from a donor site on the patient's own body), for the purpose of replacing the recipient's damaged or failing organ with a working one from the donor site. As can be seen from the above, without limitation these purposes are intended for therapeutic methods and applicant has not provided competent evidence sufficient to enable the claimed method.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make

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and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 48 and 49 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility.

As noted above in the 112 first paragraph rejection, the method of inhibiting said kinases are implicitly intended for treating various diseases. However, as recited in the amended claims appear to be for inhibiting the said enzyme in biological samples. Specification does not teach or suggest any utility of the instant compounds. Hence, the method of inhibiting said several kinases lack utility to the extent it is limited to inhibition of said kinases in biological samples.

Claims 48 and 49 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Allowable Subject Matter***

Claims 54-56 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 1-46, barring finding of any prior art in a subsequent search, would be allowed. Said claims would be allowed as prior art search in the related art did not teach or suggest instant compounds and their composition of claims 1-46 or specific method of use embraced in the objected claims 54-56.

**Conclusion**

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you

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have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

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